1653

FEE TRANSMITTAL for FY 2003 (Small Entity)

Complete if Known	
Application Number	09/666,837
Filing Date	21 September 2000
First Named Inventor	Ann H. CORNELL-BELL
Group Art Unit	1653
Examiner Name	C.M. Kam
Attorney Docket Number	2314-206

Total Amount of Payment	($) 200.00

METHOD OF PAYMENT (check one)

1. [X] The Commissioner is hereby authorized to charge additional fees and credit any overpayment to Deposit Account Number 02-2135 in the name of Rothwell, Figg, Ernst & Manbeck

   [X] Charge any Additional Fee Required Under 37 CFR 1.16 and 1.17

   [X] Applicant claims small entity status.

2. [ ] Payment Enclosed:
   - [ ] Check
   - [ ] Credit Card

FEE CALCULATION

1. FILING FEE

Fee Code	Fee $	Fee Description	Fee Paid
2001	370	Utility filing fee	[ ]
2002	165	Design Filing Fee	[ ]
2003	255	Plant Filing Fee	[ ]
2004	370	Reissue Filing Fee	[ ]
2005	80	Provisional Filing Fee	[ ]

SUBTOTAL $

2. CLAIMS

			Extra Claims		Fee	Fee Paid
Total Claims	[ ]	- 20** =	[ ]	x	$ 9 =	[ ]
Independent Claims	[ ]	- 3** =	[ ]	x	42 =	[ ]
Multiple Dependent Claims				+	140 =	[ ]

***or number previously paid, if greater;*

SUBTOTAL $

FEE CALCULATION (continued)

3. ADDITIONAL FEES

Fee Code	Fee Paid	Fee Description	Fee Paid
2051	65	Surcharge - late filing fee or oath	[ ]
2052	25	Surcharge - late provisional filing fee or cover sheet	[ ]
1053	130	Non-English specification	[ ]
1812	2,520	For filing a request for reexamination	[ ]
1804	920	Requesting publication of SIR prior to Examiner action	[ ]
1805	1,840*	Requesting publication of SIR after Examiner action	[ ]
2251	55	Extension for reply within first month	[ ]
2252	200	Extension for reply within second month	[200.00]
2253	460	Extension for reply within third month	[ ]
2254	720	Extension for reply within fourth month	[ ]
2255	980	Extension for reply within fifth month	[ ]
2401	160	Notice of Appeal	[ ]
2402	160	Filing a brief in support of an appeal	[ ]
2403	150	Request for Oral Hearing	[ ]
1451	1,510	Petition to institute a public use proceeding	[ ]
2452	55	Petition to revive -unavoidable	[ ]
2453	640	Petition to revive - unintentional	[ ]
2501	640	Utility issue fee (or reissue)	[ ]
2502	230	Design issue fee	[ ]
2503	310	Plant issue fee	[ ]
1460	130	Petitions to the Commissioner	[ ]
1807	50	Processing fee under 37 CFR 1.17(q)	[ ]
1806	180	Submission of Information Disclosure Statement	[ ]
8021	40	Recording each patent assignment per property (times number of properties)	[ ]
2809	370	Filing a submission after final rejection (37 CFR .129(a))	[ ]
2810	370	For each additional invention to be examined (37 CFR 1.129(b))	[ ]
2801	370	Request for Continued Examination (RCE)	[ ]
1802	900	Request for expedited examination of a design application	[ ]
1504	300	Publication fee for early, voluntary, or normal publication	[ ]
1505	300	Publication fee for republication	[ ]
1455	200	Filing an application for patent term adjustment	[ ]
1456	400	Request for reinstatement of term reduced	[ ]
Other fee (specify)			[ ]

* Reduced by Basic Filing Fee Paid **SUBTOTAL** $200.00

SUBMITTED BY				Complete (if applicable)	
NAME AND REG. NUMBER	Jeffrey L. Ihnen, Reg. No. 28,957				
SIGNATURE	Jeffrey L. Ihnen	DATE	24 December 2002	DEPOSIT ACCT USER ID	02-2135

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE		
	Application Number	09/666,837
	Filing Date	21 September 2000
	First Named Inventor	Ann H. CORNELL-BELL
	Group Art Unit	1646
	Examiner Name	C.M. Kam
	Attorney Docket Number	2314-206

Title of the Invention: **USES OF KAPPA-CONOTOXIN PVIIA**

RESPONSE TO RESTRICTION REQUIREMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

In the Office Action mailed 26 September 2002, the Examiner restricted the claims with respect to the individual peptides disclosed in the application. As a species of the peptide, Applicants provisionally elect the peptide PVIIA having an amino acid sequence set forth in SEQ ID NO:1 in which Xaa_1 is Arg, Xaa_2 is Hyp, Xaa_3 is Lys, Xaa_4 is Phe and Xaa_5 is His. Claims 1-8 and 10-17 read on peptide PVIIA. This election is made with traverse.

First, the Examiner alleges that "[a]ny change of amino acid residue at any one or more positions is considered, absent factual data to the contrary, a distinct peptide". However, the Examiner has not provided any valid scientific principle, reasoning, etc. that would make it likely to doubt our assertions that the peptides all have the same activity. In fact it is well known in the art relating to contoxin peptides, to which the present invention is directed, that a single class of conotoxins comprise a multiple of related peptides have the same activity with respect to sites of action. In fact, all of the peptides disclosed and claimed in the present application, including the peptides set forth in SEQ ID NOs:2-25 which are are analogs of PVIIA, all have activity against K channels.

Second, the Examiner alleges that "[e]ach peptide is patentably distinct because each sequence has different chemical property and produces different effect in the method of treatment." Again, the Examiner has not provided any evidence to establish that the claimed peptides do not all have the same disclosed property and are not all useful in the claimed method. In the absence of such evidence, the Examiner's allegations are simply not supported.

Furthermore, there are two criteria for a proper requirement for restriction between patentably distinct inventions: 1) The inventions must be independent or distinct as claimed; and 2) There must be a serious burden on the Examiner if restriction is not required. See MPEP § 803. Examiners must provide reasons and/or examples to support conclusions. For purposes of the initial requirement, a serious burden on the Examiner may be *prima facie* shown if the Examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search as defined in MPEP § 808.02. That *prima facie* showing may be rebutted by appropriate showings or evidence by the applicant. Insofar as the criteria for restriction practice relating to Markush-type claims is concerned, the criteria are set forth in MPEP § 803.02. See MPEP § 803. If the members of the Markush group are sufficiently few in number or so closely related that a search and examination of the entire claim can be made without serious burden, the Examiner must examine all claims on the merits, even though they are directed to independent and distinct inventions. In such a case, the Examiner will not require restriction. See MPEP § 803.02.

Applicants agree that the various conopeptides may be distinct from each other. However, as stated in the MPEP, as discussed above, distinctness alone is not enough to require a restriction. There must also be a serious burden upon the examiner. In the absence of such a burden, the examiner must examine all of the claims (or in this case, it is urged that all of the peptide claims should be examined). It is urged that the burden of examining all of the peptide claims of the present application is not a serious one, and that the burden of examining all of the peptide claims is only slightly greater than examining one of the groups of claims.

The examination entails various aspects. First is a decision concerning utility under 35 U.S.C. §101. Although each peptide species being claimed is distinct, they are all related in their structure and biological activity. Consequently, a decision concerning utility will be identical for all of the species, and there is no added burden of examining all of the species as compared to examining only a single species.

The second aspect of examination is whether the provisions of the various paragraphs of 35 U.S.C. § 112 have been met. In general, and in this case, this means reviewing the application and claims for compliance with the provisions of paragraphs 1 and 2 of § 112. As for the enablement aspect as found in paragraph 1 of § 112, all of the peptides are related in their structure and

biological activity. Since no basis for distinguishing between the enablement of one species vs. another species has been set forth, it is presumed that all of the listed peptides will be treated equally. Again, this means that only a single decision needs to be made concerning all of the peptides. Therefore, this aspect of the examination will not be a serious burden if all peptides are examined, vs. only one of the peptides.

Concerning paragraph 2 of § 112, this involves the wording of the claims. The wording of the claims in each group of claims is identical except for the specified peptide. Consequently, any objections to the language of the claims for one Group of claims is equally applicable to the other Groups of claims. Therefore there is no increase in the burden concerning 35 U.S.C. § 112, second paragraph, if all peptide claims are examined.

The third aspect of examination is a review of prior art to determine whether the claims are anticipated or obvious. There are two aspects of such a search. A first aspect is a review of the prior art literature and patents. The literature to be reviewed will be identical for all of the peptides. All of the claimed peptides have similar, though not identical, structures and all are claimed to have the same utility. The Examiner has not stated that a search of the scientific literature will be any different for one peptide than for any other peptide. Consequently, the search of the patent literature will clearly be the same for all of the peptides. Because the search of the scientific literature and patent literature will be identical for all of the peptides, there is no added burden concerning this aspect if all of the peptides are examined. Furthermore, the search will probably entail a computer search based on the peptide sequences in the sequence listing. It is believed that such a search would identify prior art directed to the claimed peptides or peptides having the specified substitutions.

It is Applicants understanding that the Patent Office uses BLAST as its main method of sequence searching. In the present application, the claims are directed to a relatively limited generic and a series of point mutants (mainly Alanine substitutions). Analysis of the generic SEQ ID NO:1 shows essentially the following substitutions:

C	R	I	O	N	Q	K	C	F	Q	H	L	D	D	C	C	S	R	K	C	N	R	F	N	K	C	V
	K		P			R		Y									K	R			K	Y		R		
	H					H		W									H	H			H	W		H		
	1					1		2									1	1			1	2		1		

where 1 is any basic (non-standard) amino acid and 2 is any aromatic (non-standard) amino acid. A search using BLAST is limited to searching only the standard amino acids in any case. Thus, if Applicants elected a species, GCCSNPVCH3EHSNLC, where 3 was the non-standard amino acid, Norleucine, the search would be for: GCCSNPVCHXEHSNLC, where X is for an undetermined amino acid (e.g. it matches with any residue at this position). Applying this to the generic sequence, neither Hyp (O) at position 4 nor any of the non-standard amino acids represented by 1 or 2 could be searched. Instead, X could be inserted for each of the variant positions thus searching for: CXIXNQXCXQHLDDCCSXXCNXXNXCV. This might not be an optimal search as the larger number of Xs in a short sequence lowers the likelihood of achieving relevant matches. If, however, the search is done for the native sequence, **C**RIONQK**C**FQHLDD**CC**SRK**C**NRFNK**C**V, one will get matches for positions in which, for example, R aligns with K or H, where I aligns with L or V, or F aligns with Y or W. Blast will indicate these homologous (but not identical) matches. Thus, with a single BLAST search for the native sequence, one will pull out all relevant sequences. In addition, this same search will most assuredly find EVERY single point mutant claimed in SEQ ID NO:2 through SEQ ID NO:25.

In fact, Applicants have run the proposed searches (i.e., the search with several Xs and the search of the native sequence) in order to demonstrate that a single search of the native sequence is sufficient to identify any of the claimed analogs. The searches were as follows.

1) the native PVIIA sequence (except Hyp at pos 4 was searched as Pro) against the Non-redundant Genbank database [NR Native PVIIA Search]

2) native PVIIA sequence (except Hyp at pos 4 was searched as Pro) against the Patent Genbank database [Pat Native PVIIA Search]

3) a generic PVIIA sequence (CXIXNQXCXQHLDDCCSXXCNXXNXCV) against the Non-redundant Genbank database [NR Gen PVIIA Search]

4) a generic PVIIA sequence (CXIXNQXCXQHLDDCCSXXCNXXNXCV) against the Patent Genbank database [Pat Gen PVIIA Search]

5) a very divergent PVIIA sequence (CHIXNQHCWQHLDDCCSHHCNHWNHCV - this is basically a sequence as divergent from PVIIA as could be created while still using the standard

amino acids and still be within the scope of generic SEQ ID NO:1) against the Non-redundant Genbank database [Search for: CHIXNQHCWQHLDDCCSHHCNHWNHCV]
The results of these searches are attached. In all cases, these searches found that only native PVIIA was identified as a significant match. The divergent search also only found native PVIIA as a significant match and did not identify any other peptides as significant matches. It is submitted that these searches demonstrate that the claimed subject matter can be readily searched without any serious burden on the Examiner.

Consequently, it is submitted that the only reason for restriction is that the peptides are distinct from each other. But as explicitly stated in MPEP § 803, the inventions must be distinct and there must be a serious burden on the examiner. MPEP § 803.02 states that if a search and examination of an entire claim can be made without serious burden, the examiner must examine all claims on the merits, even though they are directed to independent and distinct inventions. As urged above, it is asserted that examination of all of the peptides claims will not impose a serious burden.

In view of the above arguments, it is requested that the restriction requirement imposed in the Office Action mailed 26 September 2002 be reconsidered and that all of peptides be examined together.

<table>
<tr><td colspan="6">RESPECTFULLY SUBMITTED,</td></tr>
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<tr><td>Signature</td><td colspan="2">  </td><td>Date</td><td colspan="2">24 December 2002</td></tr>
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Attachments: Five Genbank Search Results